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The Examiner has requested that Applicants provide all non-U.S. patent references cited in the Information Disclosure Statement of provided with the Communication that was sent on July 27, 1998. Applicants have attached the references to this Response.

The Examiner has rejected Claims 21 and 13-19 under 35 U.S.C. §112, first paragraph, as containing subject matter which is not described in such a way as to enable one skilled in the art to make and/or use the invention. The Examiner suggests that because there are higher levels of PSA in the blood of persons with prostate cancer, it is not clear how the instant conjugates would avoid being cleaved in the blood prior to being cleaved at the local site of the cancer itself. The Examiner appears to require an explanation as to how the claimed conjugates would be available to treat prostate cancer.

Applicants respectfully note that the Background of the Invention as filed provides an appropriate explanation as to how the conjugates of the instant invention would be available at the site of the prostate cancer. Applicants note that it was well known at the time of the filing of the instant application that the predominant form of PSA in the serum (>95%) is as an enzymatically inhibited complex with alpha 1-antichymotrypsin (page 2, lines 10-24). Applicants also note that it was known prior to the filing of any of the remaining serum PSA is unlikely to exhibit any enzymatic activity because of the vast molar excess of unreacted alpha 1-antichymotrypsin and alpha 2-macroglobulin in serum as compared to the detected serum levels of the free PSA (page 3, lines 1-8). Applicants therefore respectfully contend that the invention of localized delivery of the cytotoxic agent upon cleavage by the enzymatically active PSA at the cancer cell site was based, at the time of the filing of the instant application, on knowledge in the art about where in the body active PSA resided. It is the Applicants' contention that such knowledge, combined with the Applicants' invention of incorporating a cleavable peptide on a cytotoxic agent would be sufficient explanation as to how the instant conjugate could be "used."

Applicants therefore contend the Examiner's rejection under 35 U.S.C. §112, first paragraph, is untenable and should be withdrawn.

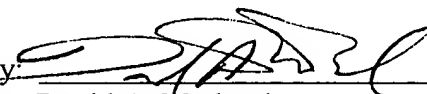
The Examiner has rejected Claims 21 and 13-19 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent

5,866,679. The Examiner suggests that the conflicting claims are not identical, but that they are not patentably distinct from each other because both the instant application and the '679 patent disclose conjugates. The Examiner also suggests however that the scope of the '679 patent and the instant claims overlaps. Applicants respectfully note that the '679 patent is directed to the pharmaceutically acceptable salts of the instantly claimed conjugates, while the instant application is directed to the conjugate free base or free acid. The Applicants therefore contend that there is no overlap between the two sets of claims.

However, in order to advance the prosecution of the instant application Applicants are herewith submitting a Terminal Disclaimer over the '679 patent. In light of the Terminal Disclaimer, Applicants contend that the rejection of Claims 21 and 13-19 under the judicially created doctrine of obviousness-type double patenting is now moot and should be withdrawn.

Applicants respectfully contend that the Examiner's rejections have been addressed and obviated by the above remarks, and that Claims 21 and 13-19 are allowable and an early Notice of Allowance is earnestly solicited. If a telephonic communication with the Applicants' representative will aid in the finding of allowability of the instant application, please telephone Mr. David A. Muthard at (908) 594-3903.

Respectfully submitted,

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